

## JOURNALSCAN

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Editor, *JournalScan*

### ISCHAEMIC HEART DISEASE

**The CURE for ACS?** Presented at the American College of Cardiology, the CURE (clopidogrel in unstable angina to prevent recurrent events) trial showed increased minor bleeding from 8.6% to 15.2%, and major bleeding from 2.7% to 3.6%. However, the primary end point for death/myocardial infarction(MI)/cerebrovascular accident was reduced from 11.5% to 9.3% at one year follow up. So for one extra bleed, two cardiovascular events are prevented per 100 patients treated. The individual end points of death and stroke were not decreased. Perhaps clopidogrel should be reserved for the higher risk acute coronary syndrome in the first instance.

*Clopidogrel in unstable angina to prevent recurrent ischemic events (CURE).* Salim Yusuf, American College of Cardiology, 50th Scientific Sessions, Orlando, Florida 2001.

**Watch out for artefact before diagnosing VT on a rhythm strip:** "An asymptomatic patient with a previous MI has an ECG". When shown an ECG rhythm strip with what looked like ventricular tachycardia (VT) and given this history, 94% of junior doctors and 58% of cardiologists failed to notice the normal QRS complexes that ran through it, confirming that the apparent VT was caused by an artefact. Electrophysiologists did better, but even 30% of them made the mistake. The worrying thing was that the incorrect diagnoses led to the suggestion of referral for invasive tests.

- 1 Knight BP, Pelosi F, Michaud GF, Strickberger SA, Morady F. Physician interpretation of electrocardiographic artifact that mimics ventricular tachycardia. *Am J Med* 2001;110:335–423.

#### Use amiodarone and $\beta$ blockade to prevent AF post-CABG:

Previous studies have shown the effectiveness of amiodarone in prevention of perioperative atrial fibrillation (AF) after coronary artery bypass graft (CABG) surgery. These data are mainly on younger patients and concomitant use of  $\beta$  blockers may have partially confounded results. In this study, elective use of perioperative amiodarone in addition to  $\beta$  blockers in older patients (> 60 years; mean age 73 years) undergoing cardiac surgery reduced the incidence of AF from 38% to 22%, as well as the risk of cerebrovascular accidents and VT (from 7% to 1.7% for each). Beginning loading as late as one day preoperatively seems adequate, and treatment was stopped on day 4 postop. Bradycardia was not a problem. This could have a major impact in reducing lengths of stay in older patients after cardiac surgery.

- 2 Giri S, White C, Dunn A, Felton K, Freeman-Bosco L, Reddy P, Tsikouris J, Wilcox H, Kluger J. Oral amiodarone for prevention of atrial fibrillation after open heart surgery: the atrial fibrillation suppression trial (AFIST). *Lancet* 2001;357:830–6.

**Yes or no to garlic?** A review of garlic to reduce cardiovascular risk concludes that there may be a small reduction in cholesterol concentrations (0.3–0.6 mmol/l at three months), but this was not sustained at six months. There are no good trials to suggest that garlic is truly better than placebo in reducing coronary heart disease risk.

- 3 Ackermann RT, Mulrow CD, Ramirez G, Gardner CD, Morbidoni L, Lawrence VA. Garlic shows promise for improving some cardiovascular risk factors. *Arch Intern Med* 2001;161:813–24.

**Early lipid lowering after ACS: retrospective evidence:** Treatment with lipid lowering drugs initiated 3–6 months after an acute coronary syndrome (ACS) reduces mortality. What about

early treatment? Data from GUSTO IIb and PURSUIT trials compared retrospectively 17 000 patients discharged without lipid lowering treatment after an ACS with 3600 who were. Despite having more standard cardiovascular risk factors, the early lipid lowering treatment group had a lower six month mortality than the diet treated group (3.5% v 1.7%). The effect was most notable if lipid lowering treatment was initiated in hospital (rather than just continued from a pre-hospital prescription) and the patient was not revascularised.

- 4 Aronow H, Topol E, Roe M, Houghtaling P, Wolski K, Lincoff A, Harrington R, Califf R, Ohman E, Kleiman N, Keltai M, Wilcox R, Vahanian A, Armstrong P, Lauer M. Effect of lipid-lowering therapy on early mortality after acute coronary syndromes: an observational study. *Lancet* 2001;357:1063–8

**Is it really a MIRACL?** To test the effect of early lipid lowering treatment, patients with ACS were started on atorvastatin 80 mg/day within four days. Low density lipoprotein (LDL) cholesterol decreased from 3.2 mmol/l to 1.9 mmol/l. This reduced the primary end point of death/non-fatal MI/resuscitated cardiac arrest/readmission with ACS by 16% at 16 weeks. Stroke rates and readmissions with ischaemic pains were both significantly reduced, but not the hard end points of death, MI or revascularisation rates at 16 weeks. So far, the evidence is that these agents are safe to give early, but more information about the benefits of high dose early statin treatment is required. The ongoing A-to-Z, PRINCESS, and PACT trials are addressing this issue.

- 5 The MIRACL investigators. Effects of atorvastatin on early recurrent ischaemic events in acute coronary syndromes. The MIRACL study. *JAMA*;2001;285:1711–18.

**Half of CHD patients are still not getting their cholesterol below 5 mmol/l.** The most recent survey of European patients with coronary heart disease suggests that obesity and diabetes are increasing, the prevalence of hypertension is stable, and that 50% of these patients are still failing to get to target lipid concentrations. The use of proven medication for secondary prevention has increased, but more needs to be done.

- 6 EUROASPIRE I & II Group. Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I & II in nine countries. *Lancet* 2001;357:995–1001.

### HYPERTENSION

#### Creatinine is an independent predictor of cardiovascular

**risk in HT:** Within the normal range, a 20  $\mu$ mol/l higher creatinine carries a 1.3 $\times$  higher cardiovascular risk, independent of diabetes, blood pressure, and left ventricular hypertrophy.

- 1 Schillaci G, Reboldi G, Verdecchia P. High-normal serum creatinine concentration is a predictor of cardiovascular risk in essential hypertension. *Arch Intern Med* 2001;161:886–91.

### GENERAL CARDIOLOGY

#### AV node ablation and pacemaker insertion is a safe

**treatment for chronic AF:** Radiofrequency ablation of the atrioventricular (AV) node and implantation of a permanent pacemaker are an alternative to drug treatment in patients with refractory atrial fibrillation (AF). All patients who underwent this procedure at the Mayo Clinic between 1990 and 1998 were studied. Long term survival is similar for patients with AF, whether they receive ablation or drug treatment for rate control.

- 1 Ozcan C, Jahangir A, Friedman PA, Patel PJ, Munger TM, Rea RF, Lloyd MA, Packer DL, Hodge DO, Hayes DL, Gersh BJ, Hammill SC, Shen W-K. Long-term survival after ablation of the atrioventricular node and implantation of a permanent pacemaker in patients with atrial fibrillation. *N Engl J Med* 2001;344:1043–51.

**Biventricular pacing may help in heart failure:** One third of patients with chronic heart failure have ECG evidence of a major intraventricular conduction delay, which may worsen left ventricular systolic dysfunction. Patients with severe heart failure and normal sinus rhythm with QRS duration of more than 150 ms, received transvenous atriobiventricular pacemakers (with leads in one atrium and each ventricle). By switching the pacemaker off and on, the effects of pacing were studied. Although technically complex, atriobiventricular pacing significantly improved exercise tolerance from 375 m in the six minute walk test to 424 m. Patients were unaware of whether pacing was on or off, but when asked which period they preferred, 85% chose the paced period, and only 4% the non-paced period.

- 2 Cazeau S, Leclercq C, Lavergne T, Walker S, Varma C, Linde C, Garrigue S, Kappenberger L, Haywood GA, Santini M, Bailleul C, Mabo P, Lazarus A, Ritter P, Levy T, McKenna W, Daubert J-C for the Multisite Stimulation in Cardiomyopathies (MUSTIC) Study Investigators. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med* 2001;**344**:873–80.

## BASIC RESEARCH

**The smooth muscle cells in atherosclerotic lesions may migrate from the circulation:** Using a heart transplanted from one strain of mice to another, a Japanese group has shown that most of the smooth muscle cells in an atherosclerotic plaque have come in from the circulation, rather than local migration and proliferation. It remains to be seen whether this is true for non-transplant atherosclerosis.

- 1 Saiura A, Sata M, Hirata Y, Nagai R, Makuuchi M. Circulating smooth muscle progenitor cells contribute to atherosclerosis. *Nature Med* 2001;**7**:382–3.

**Growth factors are not yet ready to put the cardiologist out of business:** There has yet to be a published randomised blinded placebo controlled trial of angiogenic growth factors, but over 800 patients have been treated. Celletti and colleagues suggest a note of caution, since a single dose of vascular endothelial growth factor (VEGF) increased plaque size and vascularity in both mice and rabbit models of atherosclerosis. This could lead on to plaque progression or even instability.

- 2 Celletti FL, Waugh JM, Amabile PG, Brendolan A, Hilfiker PR, Dake MD. Vascular endothelial growth factor enhances atherosclerotic plaque progression. *Nature Med* 2001;**7**:425–9.

**Growing a new heart?** After myocardial infarction, regenerative strategies require new muscle and a blood supply for that muscle. Kocher and colleagues have shown the formation of new vessels from intravenously injected human bone marrow progenitors in a rat infarct model. This seemed to preserve function in the peri-infarct zone by saving myocytes at risk. Orlic and associates show that stem cells injected directly into mice myocardium soon after an infarct can differentiate into both new myocardium and new vessels.

- 3 Kocher AA, Schuster MD, Szabolcs MJ, Takuma S, Burkhoff D, Wang J, Homma S, Edwards NM, Itescu S. Neovascularization of ischemic myocardium by human bone-marrow-derived angioblasts prevents cardiomyocyte apoptosis, reduces remodeling and improves cardiac function. *Nature Med* 2001;**7**:430–6.
- 4 Orlic D, Kajstura J, Chimenti S, Jakoniuk I, Anderson SM, Li B, Pickel J, McKay R, Nadal-Ginard B, Bodine D, Leri A, Anversa P. Bone marrow cells regenerate infarcted myocardium. *Nature* 2001;**410**:701–5.

**Anti-inflammatory therapies may improve some forms of heart failure:** Mice overexpressing TNF $\alpha$  develop heart failure and a myocarditis. If ICAM-1, a surface adhesion molecule required for cell recruitment, is also lacking, then cardiac function and survival are improved. This again points to anti-TNF treatments having potential benefits in heart failure.

- 5 Graciano AL, Bryant DD, White DJ, Horton J, Bowles NE, Giroir BP. Targeted disruption of ICAM-1, P-selecting genes improves cardiac function and survival in TNF- $\alpha$  transgenic mice. *Am J Physiol Heart Circ Physiol* 2001;**280**:H1464–71.

*Journals scanned*—American Journal of Medicine; American Journal of Physiology; Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Annals of Internal Medicine; Archives of Internal Medicine; BMJ; Canadian Medical Association Journal; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax.

*Reviewers*—C Baker, E Barnes, V Bhatia, R Desilva, M Earley, K Fox, D Gorog, G Jenkins, R Kaprielian, A Kapur, M Khan, P Lambiase, V Markides, M Poullis, P Ramrakha, J Strange, B Wasan, H Walker.

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